

## **REMARKS**

Reconsideration of this application is requested in view of the above amendments and the following remarks.

### **I. Claim Status.**

Upon entry of this Amendment, claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80 and 83-86. All cancelled claims are cancelled without prejudice or disclaimer.

Claims 14, 20, 55, 56, 72, 75, 77 and 83 have been amended without prejudice or disclaimer. Support for the amended claims is found throughout the specification. Support for "contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid" of a patient as called for in claims 14, 20, 77, and 83 is found in the specification at, e.g., page 10, lines 25-26, page 11, lines 7-8, page 15, lines 13-21.

By this Amendment, no new matter has been added to the application.

### **II. Examiner's Interview Summary.**

The Applicants and their representatives wish to thank Examiner Ballard and SPE Andres for the courtesies extended at the personal interview conducted at the Patent and Trademark Office on June 27, 2006. Present at the interview were Dr. Daniel Chain (inventor of the present application) and Applicants' representatives Mitchell Bernstein and Peter Ludwig.

During the interview Dr. Chain presented an explanation of the invention and the benefits of using free-end specific antibodies to target soluble amyloid  $\beta$  peptides to inhibit accumulation of amyloid  $\beta$  in the brain.

Applicants' representatives presented possible claim amendments that would address all outstanding claim rejections. It was agreed that amending claims to call for treating Alzheimer's disease would overcome the outstanding section 112 rejection. Applicants' representatives explained that claims calling for free end specific antibodies specific for a free N-terminus of  $\beta$ -amyloid peptide or the free C-terminus of A $\beta$ 1-42 were neither anticipated by nor obvious over König. The possibility of amending the claims to call for "contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid" of a patient was discussed at length. Applicants' presented their position

that such claims are entitled to the priority of provisional application 60/041,850, filed April 9, 1997. It was noted that the prior art documents by Schenk, Bard, Frenkel and Su that are cited in the pending application were all available only after the date of the aforementioned provisional application and, thus, would not be prior art to any claims entitled to the priority of the provisional application.

The meaning of the claim term “free end specific antibody” was discussed in view of Bard. It was pointed out that the term “free end specific antibody” (as employed in the present application) refers to an antibody that binds to a free end of  $\beta$ -amyloid peptide but does not bind to APP. It was also pointed out that Bard fails to explicitly disclose such antibodies and that neither Frenkel nor Su provides evidence Bard’s antibodies are inherently free end specific antibodies.

A pending application of Rosenthal et al. (application no. 10/683,815) was drawn to the attention of the Examiners.

The Examiners indicated that points raised by Applicants’ representatives would be fully considered upon submission of Applicants’ response to the pending Office Action. The instant response is believed to adopt Applicants’ proposed claim amendments and positions that were put forth during the interview.

### **III. Priority.**

The Examiner has indicated that the effective priority date of the instant application is considered to be the filing date of 28 February 2002. In response, without conceding the Examiner’s position, the claims have been amended to claim methods that call for contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid of an Alzheimer’s patient. The amended claims are entitled to a priority date of April 9, 1997, based on priority claimed to prior applications no. 09/402,820, which is the national stage of PCT/US98/06900, filed April 9, 1998, and provisional application no. 60/041,850, filed April 9, 1997.

Support for treating Alzheimer’s disease by contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid of an Alzheimer’s patient is found in provisional application 60/041,850 at, e.g., page 10, lines 15-21 (“[antibodies] end specific for the N-terminus or C-terminus of amyloid- $\beta$

peptides, [prevent] the accumulation of amyloid- $\beta$  peptides in the cerebrospinal fluid and the aggregation of such peptides into amyloid deposits in the brain”) and at page 13, lines 17-26, which reads:

The method for preventing or inhibiting the progression of Alzheimer’s Disease in accordance with the present invention, involves delivering the gene encoding the antisenilin molecule into brain cells where antisenilins are then stably expressed and secreted into the cerebrospinal fluid. The secretion of antisenilins into the cerebrospinal fluid, where soluble A $\beta$  peptides are present, promotes the formation of soluble antisenilin-A $\beta$  complexes. These soluble antisenilin-A $\beta$  complexes are cleared from the central nervous system...

Support for treating Alzheimer’s disease by contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid of an Alzheimer’s patient is also found in prior application no. 09/402,820, which is the national stage of PCT/US98/06900, filed April 9, 1998, at, e.g., page 10, lines 19-28 and page 8, lines 5-13, and in the instant application at, e.g., page 10, lines 25-26, page 11, lines 7-8, page 15, lines 13-21.

Thus, the presently amended claims to treating Alzheimer’s disease by contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid of an Alzheimer’s patient find support in the instant application and each of the prior applications from which the instant application claims priority, up to and including provisional application no. 60/041,850. Accordingly, the instant claims are entitled to a priority date that is the filing date of the provisional application, i.e., April 9, 1997.

**IV. Claim Objections.** The Examiner has objected to claims 89-92 as substantial duplicates of claims 14, 20, 77 and 83, respectively. In response, without conceding the validity of the objection, claims 89-92 have been cancelled, without prejudice or disclaimer. The basis of the objection has been addressed and the objection should be withdrawn.

**V. Claim Rejections.** The rejections set forth in the Office Action are summarized and addressed as follows.

*(i) Rejections Under 35 U.S.C. §112, first paragraph (enablement).* Claims 14, 19, 20, 25, 51, 52, 55, 56, 59, 60, 63, 64 and 71-92 were rejected for alleged lack of enablement. The Examiner's position is that the specification does not enable the full scope of the methods called for in the claims. In response, without conceding the Examiner's position or the validity of the rejection, the claims have been amended to call for methods of inhibiting accumulation or neurotoxicity of amyloid  $\beta$  peptide in a patient suffering from Alzheimer's disease. See claims 14, 20, 77 and 83. The Examiner has acknowledged that the specification is enabling for methods for inhibiting accumulation or neurotoxicity of amyloid  $\beta$  peptide in a patient suffering from Alzheimer's disease. Office Action at page 3. Accordingly, in light of this amendment, the Examiner is requested to withdraw the instant rejection.

*(ii) Rejections Under 35 U.S.C. 102.*

(a) Claims 14, 19, 20, 25, 59, 60, 63, 64, 71-74, 76, 77, 80, 82, 83, 86 and 88-92 were rejected as allegedly anticipated under section 102(b) by König, et al., U.S. Patent No. 5,786,180 ("König") as evidenced by Solomon, et al., Proc. Natl. Acad. Sci. USA 94:4109-4112 (1997). According to the Examiner, König discloses a monoclonal antibody specific for the C-terminus of A $\beta$ 1-42 for the treatment of Alzheimer's disease.

In response, without conceding the validity of the rejection, the claims have been amended to be limited to free end specific antibodies that are targeted to a free N-terminus of amyloid  $\beta$  peptide or a free C-terminus of amyloid  $\beta$  peptide A $\beta$ 1-40. Additionally, the claims have been amended to call for contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid of an Alzheimer's patient. König does not disclose an antibody that is free-end specific for either a free N-terminus of amyloid  $\beta$  or a free C-terminus of A $\beta$ 1-40. Nor does König disclose contacting circulating amyloid  $\beta$  peptide of an Alzheimer's patient with any antibody. Accordingly, König does not anticipate the instant claims. Reconsideration of the claims and withdrawal of the rejection thereof as anticipated by König is requested.

(b) Claims 14, 19, 20, 25, 51, 52, 55, 56, 81, 87, 89 and 90 were rejected as allegedly anticipated under section 102(b) by Bard et al., Nature Med. 6:916-919 (2000), as evidenced by Su et al., J. Neurosci. Res. 53:177-186 (1998) and Frenkel et al., J. Neuroimmunol. 88:85-90 (1998). In response, without conceding the validity of the rejection, the claims have been directed to methods that call for contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid of an Alzheimer's patient. As set forth above in section III, the amended claims are entitled to a priority date of April 9, 1997. Bard was published in August 2000, i.e., after the priority date of the amended claims. Accordingly, Bard is not prior art to the amended claims. Thus, the present rejection should be withdrawn.

(c) Claims 14, 19, 20, 25, 51, 52, 55, 56, 59, 60, 63, 64, 71-77, 80-83 and 86-92 are rejected under section 102(e) as anticipated by Schenk, U.S. Patent No. 6,787,637. In response, without conceding the validity of the rejection, the claims have been directed to methods that call for contacting soluble amyloid  $\beta$  peptide in the cerebrospinal fluid of an Alzheimer's patient. As set forth above in section III, the amended claims are entitled to a priority date of April 9, 1997. Schenk has an earliest claimed priority date of May 28, 1999, i.e., after the priority date of the amended claims. Accordingly, Schenk is not prior art to the amended claims. Thus, the present rejection should be withdrawn.

(iii) Rejections Under 35 U.S.C. §103. Claims 63, 64, 71 and 72 are rejected as allegedly obvious over Schenk in view of Saido et al., Neurosci. Lett. 215:173-176 (1996) and Harigaya et al., Biochem. Biophys. Res. Comm. 276:422-427 (2000). For the reasons set forth immediately above, Schenk is not prior art to the pending claims. Nor is Harigaya prior art to the pending claims. Thus, the present rejection should be withdrawn.

For at least the reasons set forth, all pending rejections are believed to have been addressed and overcome. Reconsideration of all pending claims and withdrawal of all pending rejections thereof is requested.

**CONCLUSION**

This application is believed to be in condition for allowance, which is earnestly solicited.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact Applicants' representative at the telephone number indicated below.

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Respectfully submitted,

By 

Mitchell Bernstein, Ph.D.

Registration No.: 46,550

DARBY & DARBY P.C.

P.O. Box 5257

New York, New York 10150-5257

(212) 527-7700

(212) 527-7701 (Fax)

Attorneys/Agents For Applicant